

What Is Claimed Is:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

5 (a) a nucleotide sequence encoding the full-length death domain containing receptor polypeptide (DR3-V1) having the complete amino acid sequence in Figure 1 (SEQ ID NO:2);

(b) nucleotide sequence encoding the full-length death domain containing receptor (DR3) polypeptide having the complete amino acid sequence
10 in Figure 2 (SEQ ID NO:4), including the predicted leader sequence;

(c) a nucleotide sequence encoding the DR3-V1 polypeptide having the amino acid sequence at positions from about 36 to about 428 in Figure 1 (SEQ ID NO:2);

(d) a nucleotide sequence encoding the full-length DR3-V1
15 polypeptide having the complete amino acid sequence including the leader encoded by the cDNA clone contained in ATCC Deposit No. 97456;

(e) a nucleotide sequence encoding the full-length DR3 polypeptide having the complete amino acid sequence including the leader encoded by the cDNA clone contained in ATCC Deposit No. 97757;

20 (f) a nucleotide sequence encoding the mature DR3-V1 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97456;

(g) a nucleotide sequence encoding the mature DR3 polypeptide having the amino acid sequence encoded by the cDNA clone
25 contained in ATCC Deposit No. 97757;

(h) a nucleotide sequence that encodes the DR3 extracellular domain;

(i) a nucleotide sequence that encodes the DR3 transmembrane domain;

(j) a nucleotide sequence that encodes the DR3 intracellular domain;

5 (k) a nucleotide sequence that encodes the DR3 death domain; and

(l) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j) or (k).

10 2. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence in Figure 1 (SEQ ID NO:1).

3. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 1 (SEQ ID NO:1) encoding the death domain containing receptor polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2).

15 4. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 1 (SEQ ID NO:1) encoding the mature death domain containing receptor polypeptide having the amino acid sequence in Figure 1 (SEQ ID NO:2).

20 5. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No. 97456.

6. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence in Figure 2 (SEQ ID NO:3).

7. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 1 (SEQ ID NO:1) encoding the death domain containing receptor polypeptide having the complete amino acid sequence in Figure 1 (SEQ ID NO:2).

5 8. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence in Figure 2 (SEQ ID NO:3) encoding the mature death domain containing receptor polypeptide having the amino acid sequence in Figure 2 (SEQ ID NO:4).

10 9. The nucleic acid molecule of claim 1 wherein said polynucleotide has the complete nucleotide sequence of the cDNA clone contained in ATCC Deposit No.97757.

15 10. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the death domain containing receptor polypeptide having the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97456.

11. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the mature death domain containing receptor polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97456.

20 12. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the death domain containing receptor polypeptide having the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97757.

13. The nucleic acid molecule of claim 1 wherein said polynucleotide has the nucleotide sequence encoding the mature death domain containing receptor polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97757.

5

14. An isolated nucleic acid molecule comprising a polynucleotide which hybridizes under stringent hybridization conditions to a polynucleotide having a nucleotide sequence identical to a nucleotide sequence in (a), (b), (c), (d), (e), (f), (g), (h), (i), (j), (k) or (l) of claim 1 wherein said polynucleotide which
10 hybridizes does not hybridize under stringent hybridization conditions to a polynucleotide having a nucleotide sequence consisting of only A residues or of only T residues.

15. An isolated nucleic acid molecule comprising a polynucleotide which encodes the amino acid sequence of an epitope-bearing portion of a death domain containing receptor polypeptide having an amino acid sequence in (a), (b),
15 (c), (d), (e), (f), (g), (h), (i), (j) or (k) of claim 1.

16. The isolated nucleic acid molecule of claim 15, which encodes an epitope-bearing portion of a death domain containing receptor polypeptide selected from the group consisting of: a polypeptide comprising amino acid
20 residues from about 1 to about 22 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from about 33 to about 56 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from about 59 to about 82 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from
25 about 95 to about 112 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from about 122 to about 133 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from about 161 to about 177 in Figure 1 (SEQ ID NO:2); a polypeptide comprising amino acid residues from

about 179 to about 190 in Figure 1 (SEQ ID NO:2); and a polypeptide comprising amino acid residues from about 196 to about 205 in Figure 1 (SEQ ID NO:2).

5 17. A method for making a recombinant vector comprising inserting an isolated nucleic acid molecule of claim 1 into a vector.

18. A recombinant vector produced by the method of claim 17.

10 19. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 18 into a host cell.

20. A recombinant host cell produced by the method of claim 19.

15 21. A recombinant method for producing a death domain containing receptor polypeptide, comprising culturing the recombinant host cell of claim 20 under conditions such that said polypeptide is expressed and recovering said polypeptide.

22. An isolated death domain containing receptor polypeptide having an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

20 (a) the amino acid sequence of the DR3-V1 polypeptide having the complete 428 amino acid sequence, including the leader sequence shown in Figure 1 (SEQ ID NO:2);

 (b) the amino acid sequence of the DR3 polypeptide having the complete 417 amino acid sequence, including the leader sequence, shown in Figure 2 (SEQ ID NO:4);

(c) the amino acid sequence of the DR3-V1 polypeptide having the amino acid sequence at positions from about 36 to about 428 in Figure 1 (SEQ ID NO:2);

5 (d) the amino acid sequence of the DR3-V1 polypeptide having the complete amino acid sequence, including the leader, encoded by the cDNA clone contained in ATCC Deposit No. 97456;

(e) the amino acid sequence of the DR3 polypeptide having the complete amino acid sequence, including the leader, encoded by the cDNA clone contained in ATCC Deposit No. 97757;

10 (f) the amino acid sequence of the mature DR3 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97456;

(g) the amino acid sequence encoding the mature DR3 polypeptide having the amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97757;

(h) the amino acid sequence of the DR3 extracellular domain;

(i) the amino acid sequence of the DR3 transmembrane domain;

(j) the amino acid sequence of the DR3 intracellular domain;

20 (k) the amino acid sequence of the DR3 death domain; and

(l) the amino acid sequence of an epitope-bearing portion of any one of the polypeptides of (a), (b), (c), (d), (e), (f), (g), (h), (i), (j) or (k).

23. An isolated antibody that binds specifically to a death domain containing receptor polypeptide of claim 22.

25 24. A method of treating diseases and disorders associated with the inhibition of apoptosis comprising administering an effective amount of the

polypeptide as claimed in claim 22, or an agonist thereof to a patient in need thereof.

5 25. A method of treating diseases and disorders associated with increased apoptosis comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 22 to a patient in need thereof.

 26. A method of treating inflammatory diseases and disorders comprising administering to a patient in need thereof an effective amount of an antagonist of the polypeptide as claimed in claim 22.

11/11/81